REMARKS

Status of the Claims

Pending claims

Claims 1 to 60 as filed are pending.

Claims amended and added in the instant amendment

Claims 51, 52 and 59 are amended and claims 61 to 69 are added. Thus, after entry of the instant amendment, claims 1 to 69 will be pending.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to compositions and methods comprising bioluminescence imaging can be found, inter alia, on page 8, lines 11 to 22, and page 14, line 10 to page 15, line 9.

The Restriction Requirement

The Patent Office has alleged that the pending claims of the application are directed to twenty separate and distinct inventions under 35 U.S.C. §121:

Group I: Claims 1-9, and 16-44, drawn to a chimeric polypeptide molecule comprising RGD motif polypeptide comprises SEQ ID NO: 1 and pharmaceutical formulation thereof, classified in Class 530, subclass 350; class 514, subclass 2.

Group II: Claims 1-4, 10, 11, and 16-44, drawn to a chimeric polypeptide molecule comprising E-selectin binding polypeptide comprises SEQ ID NO: 2 and pharmaceutical formulation thereof; classified in Class 530, subclass 350; class 514, subclass 2.

Group III: Claims 1-4, 12, 13, and 16-44, drawn to a chimeric polypeptide molecule comprising MMP comprises SEQ ID NO:3 polypeptide and pharmaceutical formulation thereof, classified in Class 530, subclass 350; class 514, subclass 2.

Group IV: Claims 1-4, and 14-44, drawn to a chimeric polypeptide molecule comprising proteoglycan binding polypeptide comprises SEQ ID NO: 4 and pharmaceutical formulation thereof, classified in Class 530, subclass 350; class 514, subclass 2.

Group V: Claims 1-4, and 15-44, drawn to a chimeric polypeptide molecule comprising proteoglycan binding polypeptide comprises SEQ ID NO: 5 and pharmaceutical formulation thereof, classified in Class 530, subclass 350; class 514, subclass 2.

Group VI: Claims 45-50, drawn to a nucleic acid encoding chimeric RGD polypeptide comprises SEQ ID NO: 1, vector and host cells and pharmaceutical formulation thereof, classified in Class 536, subclass 23.4; Class 435, subclasses 69.1, 252.3, and 320.1.

Group VII: Claims 45-50, drawn to a nucleic acid encoding chimeric E-selectin polypeptide comprises SEQ ID NO: 2, vector and host cells, classified in Class 536, subclass 23.4; Class 435, subclasses 69.1, 252.3, and 320.1.

Group VIII: Claims 45-50, drawn to a nucleic acid encoding chimeric MMP polypeptide comprises SEQ ID NO: 3, vector and host cells, classified in Class 536, subclass 23.4; Class 435, subclasses 69.1, 252.3, and 320.1.

Group IX: Claims 45-50, drawn to a nucleic acid encoding chimeric chondroitin sulfate proteoglycan polypeptide comprises SEQ ID NO: 4, vector and host cells, classified in Class 536, subclass 23.4; Class 435, subclasses 69.1, 252.3, and 320.1.

Group X: Claims 45-50, drawn to a nucleic acid encoding chimeric chondroitin sulfate proteoglycan polypeptide comprises SEQ ID NO: 5, vector and host cells, classified in Class 536, subclass 23.4; Class 435, subclasses 69.1, 252.3, and 320.1.

Group XI: Claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising RGD polypeptide comprises SEQ ID NO: 1 chimeric molecule, class 424, subclass 138.1 and 146.1.

Group XII: Claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising E-selectin binding polypeptide comprises SEQ ID NO: 2 chimeric molecule, class 424, subclass 138.1 and 146.1.

Group XIII: Claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising MMP comprises SEQ ID NO: 3 chimeric molecule, class 424, subclass 138.1 and 146.1.

Group XIV: Claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising chondroitin sulfate proteoglycan binding polypeptide comprises SEQ ID NO: 4 chimeric molecule, class 424, subclass 138.1 and 146.1.

Group XV: Claims 51-59, drawn to methods of in situ and in vivo imaging comprising chondroitin sulfate proteoglycan binding polypeptide comprises SEQ ID NO: 5 chimeric molecule, class 424, subclass 138.1 and 146.1.

Group XVI: Claim 60, drawn to a method of screening comprising RGD binding polypeptide comprises SEQ ID NO: 1 chimeric molecule; classified in Class 435, subclass 7.1.

Group XVII: Claim 60, drawn to a method of screening comprising E-selectin binding polypeptide comprises SEQ ID NO: 2 chimeric molecule; classified in Class 435, subclass 7.1.

Group XVIII: Claim 60, drawn to a method of screening comprising MMP binding polypeptide comprises SEQ ID NO: 3 chimeric molecule; classified in Class 435, subclass 7.1.

Group XIX: Claim 60, drawn to a method of screening comprising chondroitin sulfate proteoglycan binding polypeptide comprises SEQ ID NO: 4 chimeric molecule; classified in Class 435, subclass 7.1.

Group XX: Claim 60, drawn to a method of screening comprising chondroitin sulfate proteoglycan binding polypeptide comprises SEQ ID NO: 5 chimeric molecule; classified in Class 435, subclass 7.1.

The Election

In response to the Restriction Requirement, Applicants elect Group XI, claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising an RGD polypeptide comprising SEQ ID NO: 1 chimeric molecule, class 424, subclass 138.1 and 146.1, with traverse.

Applicants respectfully note that claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising an RGD polypeptide, are not limited to compositions comprising the exemplary SEQ ID NO:1.

Reasons to reconsider and withdraw restriction requirement

Applicants respectfully request the Patent Office to reconsider and to withdraw, in part, the restriction requirement for the following reasons.

Applicants also respectfully request that the Patent Office reconsider the restriction requirement and rejoin Groups I, XI and XVI because a search directed to any of these Groups would encompass a search for chimeric molecules comprising an RGD molecule and it would not be an undue burden for the Patent Office also to search for novel uses for these compositions, e.g., methods for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body, methods for *in vivo* imaging a tumor neovasculature in an individual, method for *in vivo* screening for an anti-tumor agent by imaging a tumor neovasculature in an individual.

Applicants also respectfully request that the Patent Office reconsider the restriction requirement and rejoin Groups II, XII and XVII because a search directed to any of these Groups would encompass a search for chimeric molecules comprising a E-selectin binding polypeptides and it would not be an undue burden for the Patent Office to search for these groups together and also to search for novel uses for these compositions, e.g., methods for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body, methods for *in vivo* imaging a tumor neovasculature in an individual, method for *in vivo* screening for an anti-tumor agent by imaging a tumor neovasculature in an individual.

Applicants also respectfully request that the Patent Office reconsider the restriction requirement and rejoin Groups III, XIII and XVIII because a search directed to any of these Groups would encompass a search for chimeric molecules comprising matrix metalloproteinase (MMP)-binding polypeptides and it would not be an undue burden for the Patent Office to search for these groups together and also to search for novel uses for these compositions, e.g., methods for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body, methods for *in vivo* imaging a tumor neovasculature in an individual, method for *in vivo* screening for an anti-tumor agent by imaging a tumor neovasculature in an individual.

Applicants also respectfully request that the Patent Office reconsider the restriction requirement and rejoin Groups IV, V, XIV, XV, XIX and XX because a search directed to any of these Groups would encompass a search for chimeric molecules comprising chondroitin sulfate proteoglycan-binding polypeptides and it would not be an undue burden for the Patent Office to search for these groups together and to search for novel uses for these compositions, e.g., methods for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body, methods for *in vivo* imaging a tumor neovasculature in an individual, method for *in vivo* screening for an anti-tumor agent by imaging a tumor neovasculature in an individual.

The Species

The Patent Office has further alleged that because the claims are directed to patentably distinct species a species election must be made. In the event Applicants elect either of Groups I, II, III or IV, a species election is required for:

A) Fluorescent

B) bioluminescent
C) radioactive isotope
D) paramagnetic
E) chemiluminescent
F) heterologous kinase

The Species Election

Applicants have elected Group XI, claims 51-59, drawn to methods of *in situ* and *in vivo* imaging comprising an RGD polypeptide comprising a chimeric molecule.

However, Applicants have requested reconsideration of the restriction requirement and rejoining of Group I and/or Group VIII with Group XI. Upon rejoining of Group I to Group XI, Applicants elect species E) chemiluminescent, e.g., luciferase.

When the elected species is held to be allowable, Applicants are entitled to consideration (examination) of additional species; if all species are held to be allowable, a generic claim should be allowed (MPEP §809.02(c); pg 800-50, 8th Edition, August 2001).

If additional fees are required, the Commissioner is authorized to deduct such fees from the undersigned's Deposit Account No. 06-1050. Please credit any overpayment to the above-noted Deposit Account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 678 5070.

Respectfully submitted,

Date May 13, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant : Arul M. Chinnaiyan, et al. Art Unit : Maher M. Haddad
Serial No. : 09/734,628 Examiner : 1644
Filed : December 11, 2000
Title : COMPOSITIONS AND METHODS FOR IN SITU AND IN VIVO IMAGING OF CELLS AND TISSUES

In The Claims:

The claims have been amended as follows:

51. (Amended) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising administration of a pharmaceutical formulation in an amount sufficient to enhance the image,

wherein the pharmaceutical formulation comprises a composition [as set forth in claim 18] comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a fluorescent, bioluminescent or chemiluminescent polypeptide, or a heterologous kinase, and a second domain comprising a member selected from the group consisting of an RGD motif-comprising polypeptide; a selectin-binding polypeptide; a matrix metalloproteinase (MMP)-binding polypeptide, and a chondroitin sulfate proteoglycan-binding polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI),

wherein the image is generated by computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence imaging (BLI) or equivalent.

52. (Amended) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising the following steps:

(a) providing a pharmaceutical formulation [as set forth in claim 18] comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a fluorescent, bioluminescent or chemiluminescent polypeptide, or a heterologous kinase, and a second domain comprising a member selected from the group consisting of an RGD motif-comprising polypeptide; a selectin-binding polypeptide; a matrix metalloproteinase (MMP)-binding polypeptide, and a chondroitin sulfate proteoglycan-binding polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is a computer assisted tomography (CAT) device, a magnetic resonance spectroscopy (MRS) device, a magnetic resonance imaging (MRI) device, a positron emission tomography (PET) device, a single-photon emission computed tomography (SPECT) device, a bioluminescence imaging (BLI) device or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to generate the cell, tissue or body image; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the cell, tissue or body.

59. (Amended) A method for *in vivo* imaging a tumor neovasculature in an individual comprising the following steps:

(a) providing a pharmaceutical formulation [as set forth in claim 18] comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a fluorescent, bioluminescent or chemiluminescent polypeptide, or a heterologous kinase, and a second domain

comprising a member selected from the group consisting of an RGD motif-comprising polypeptide; a selectin-binding polypeptide; a matrix metalloproteinase (MMP)-binding polypeptide, and a chondroitin sulfate proteoglycan-binding polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence image (BLI) or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to image the tumor neovasculature; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the tumor neovasculature.

The following new claims have been added:

--61. (NEW) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising administration of a pharmaceutical formulation in an amount sufficient to enhance the image,

wherein the pharmaceutical formulation comprises a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging polypeptide and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a

positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI),

wherein the image is generated by computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence imaging (BLI) or equivalent.

62. (NEW) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising the following steps:

(a) providing a pharmaceutical formulation comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging polypeptide and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is a computer assisted tomography (CAT) device, a magnetic resonance spectroscopy (MRS) device, a magnetic resonance imaging (MRI) device, a positron emission tomography (PET) device, a single-photon emission computed tomography (SPECT) device, a bioluminescence imaging (BLI) device or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to generate the cell, tissue or body image; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the cell, tissue or body.

63. (NEW) A method for *in vivo* imaging a tumor neovasculature in an individual comprising the following steps:

(a) providing a pharmaceutical formulation comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging polypeptide and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence image (BLI) or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to image the tumor neovasculature; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the tumor neovasculature.

64. (NEW) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising administration of a pharmaceutical formulation in an amount sufficient to enhance the image,

wherein the pharmaceutical formulation comprises a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging means and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an

amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI),

wherein the image is generated by computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence imaging (BLI) or equivalent.

65. (NEW) A method for *in situ* or *in vivo* imaging of a cell, a tissue, an organ or a full body comprising the following steps:

(a) providing a pharmaceutical formulation comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging means and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is a computer assisted tomography (CAT) device, a magnetic resonance spectroscopy (MRS) device, a magnetic resonance imaging (MRI) device, a positron emission tomography (PET) device, a single-photon emission computed tomography (SPECT) device, a bioluminescence imaging (BLI) device or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to generate the cell, tissue or body image; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the cell, tissue or body.

66. (NEW) A method for *in vivo* imaging a tumor neovasculature in an individual comprising the following steps:

(a) providing a pharmaceutical formulation comprising a chimeric molecule and a pharmaceutically acceptable excipient, wherein the chimeric molecule comprises a first domain comprising a bioluminescence imaging means and a second domain comprising an RGD motif-comprising polypeptide, and the formulation is suitable for administration as an imaging enhancing agent and the chimeric molecule is present is an amount sufficient to enhance a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI);

(b) providing an imaging device

wherein the imaging device is computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence image (BLI) or equivalent;

(c) administering the pharmaceutical formulation in an amount sufficient to image the tumor neovasculature; and,

(d) imaging the distribution of the pharmaceutical formulation of step (a) with the imaging device, thereby imaging the tumor neovasculature.

67. (NEW) The method of claim 51, claim 52, or claim 59, wherein the RGD motif-comprising polypeptide comprises a sequence as set forth in SEQ ID NO:1.

68. (NEW) The method of claim 61, claim 62, or claim 63, wherein the RGD motif-comprising polypeptide comprises a sequence as set forth in SEQ ID NO:1.

69. (NEW) The method of claim 64, claim 65, or claim 66, wherein the RGD motif-comprising polypeptide comprises a sequence as set forth in SEQ ID NO:1.--